Ch 2, part 1: Cell Respiration & Cell Metabolism

Objectives:

1. Understand what molecules our cells metabolize for energy.
   - Carbohydrates (first!)
   - Lipids (next)
   - Amino acids (routine & emergency)
   - Lactic acid (routine & emergency)

2. Understand the basics of cell respiration.

3. Become familiar with anaerobic & aerobic cell respiration


1. Types of Cell Metabolism

   i) Carbohydrate metabolism – making or breaking down carbohydrates (ex. Glucose and glycogen).

   ii) Lipid metabolism – making or breaking down lipids (ex. Ketones, fatty acids, triglycerides)

   iii) Protein metabolism (amino acids) – making or breaking down protein.

   iv) Lactic acid metabolism – making or breaking down lactic acid.
**Glucose metabolism:**

Glycolysis = use of glucose for making ATP during cell respiration.

**Glycogen metabolism:**

Glycogenesis = making of glycogen from glucose molecules. "genesis" = to create

Glycogenolysis = breaking down glycogen into glucose. "lysis" = to break apart

(Ques: what do you remember from Ch 1 about this process? What pancreatic hormone can stimulate this in the liver?)

**Lipid metabolism:**

Lipogenesis = making lipids (from extra glucose) such as ketones, fatty acids, & triglycerides, to store energy in fat cells and the liver.

Lipolysis = breaking down lipids, like triglycerides, into fatty acids & ketones to use for energy.

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**Glycogenesis = creation of glycogen from glucose molecules**

Glucose + glucose $\rightarrow$ Glycogen

(enzyme in liver & skeletal muscle)

**Glycogenolysis = breakdown of glycogen into glucose**

Glycogen $\rightarrow$ glucose 6-phosphate $\rightarrow$ free glucose

(enzyme in liver only!)

"ase" = enzyme 
"synthesis" = to create

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4
Glycogen metabolism

If insulin is present the liver takes up blood glucose and can undergo glycogenesis.

Glucose + Glucose → Glycogen

What enzyme is needed for this to happen?

Glycogen synthase

If glucagon is present, the liver can breakdown glycogen into free glucose (glycogenolysis)

Glycogen → Glucose 6 phosphate → free glucose

What enzyme is needed for this to happen?

Glycogen phosphorylase

What enzyme does the liver have (but not skeletal muscles) for this to happen?

Glucose 6 phosphatase

2. Basics of Cell Respiration – use of glucose in cell respiration:
Pg 27 – 29 Wiki text

Glycolysis
= 1st step in use of glucose for cell respiration
to make ATP

- Occurs in cell cytoplasm

- Conversion of 1 glucose molecule into:
  > 2 pyruvate main product
  > 2 NADHside products
  > 2 ATP

Pyruvate then can go one of 2 ways
- depends on if O2 is present or not
Pyruvate from glycolysis then can go one of 2 ways - depends on if O\textsuperscript{2} is present or not

- **Anaerobic respiration**
- **Fermentation**

Products = 
- Pyruvate Processing
- The Krebs cycle
- ETC

Products = 34 - 36 ATP

**Ischemia, Serum Lactate, and Heart Attack**

Ischemia & Angina Pectoris – Click HERE for Clinical App reading.

“Ischemia” = loss of blood supply

**Loss of blood flow to heart:**
- without arterial blood & O2 heart resorts to anaerobic respiration. Loss of blood & O2 to heart can cause ...

“angina pectoris” = pain associated with loss of O2 supply to heart.
- Prelude to “myocardial infarction” (heart attack)

- Normal serum lactate = 1- 0.5 mmol/L
- **Hyperlactatemia** (high serum lactate) = > 4mmol/L

Serum Lactate as a Marker of Acute Myocardial Infarction
Aerobic respiration

3 Steps of aerobic respiration (AFTER GLYCOLYSIS):
1. Pyruvate processing (pyruvate conversion)
   2 pyruvate enter → 2 Acetyl CoA, 2 NADH, 2 CO₂

2. Kreb’s cycle (citric acid cycle)
   2 Acetyl CoA enter → 2 ATP, 6 NADH, 2 FADH₂, 4 CO₂

3. Electron transport chain (ETC)
   2 NADH, 6 NADH, 2 FADH₂ enter → 30 – 32 ATP, 10 NAD⁺, 2 FAD⁺, 12 H₂O

Numerous

Fewer
Electron Transport Chain within the cell mitochondria – ATP production!
Click [HERE](#) to see GIF online.

Question:
Why do we need oxygen???

= As final electron acceptor in ETC in production of ATP!

Click [HERE](#) for blank flow diagram.
Click [HERE](#) for key.
When aerobic respiration goes wrong!

Read online Clinical App: cyanide
Review

- Our cells can metabolize carbohydrates, lipids, protein, and lactic acid
- Carbohydrate metabolism includes:
  - Glucose metabolism for ATP (glycolysis during cell respiration)
  - Glycogen metabolism
    - Making glycogen (glycogenesis), requires enzyme glycogen synthase
    - Breaking down glycogen (glycogenolysis), requires enzyme glycogen phosphorylase in skeletal muscle & liver, and glucose 6 phosphatase in liver.
- Glycolysis is conversion of glucose into 2 ATP, 2 NADH2, and 2 pyruvate
- Pyruvate can either go through aerobic respiration or anaerobic respiration
- In aerobic respiration, pyruvate goes thru pyruvate conversion to make 2 Acetyl CoA, 2 NADH2, 2 COS
- 2 Acetyl CoA enters Krebs cycle to make 6 NADH2, 2 FADH2, 4 CO2
- H ions enter electron transport chain to make ~ 30 – 32 ATP, 6 NADH+, 2 NADH+, and 12 H2O.
- Altogether aerobic respiration of 1 glucose yields 32 – 34 ATP

Metabolism of carbohydrates, lactic acid, lipids, & amino acids.

Gluconeogenesis = creation of glucose from non-carbohydrate sources.
(include making glucose from lactic acid, lipids, amino acids)

What conditions occur to make following happen in body?

- Lactic acid metabolism occurs when
  - when body lacks carbohydrates, and causes cells to break down lipids for energy.
  - Skeletal muscle activity (heavy use)
- Lipogenesis occurs when
  - you have excess glucose to use. Adipose and liver cells convert glucose into lipids.
- Lipolysis occurs
  - when body lacks carbohydrates, and causes cells to break down lipids for energy.
- Amino acid metabolism occurs
  - when consume protein, or with heavy skeletal muscle use, or during starvation.
Lactic acid (lactate) metabolism = “The Cori cycle”

= lactic acid (from skeletal muscle activity & anaerobic respiration) can cause “metabolic acidosis” and drive blood pH ↓.

Liver “recycles” lactic acid in blood into:

- **Free glucose** (to be returned to blood stream)
  - (due to enzyme only in liver – glucose 6 phosphatase)
- Stored **glycogen** (for future need)
- Reverses metabolic acidosis

What is the term for when non-carbohydrate molecules (like lactic acid) are turned into glucose?  **Gluconeogenesis!**

**Lipid Metabolism:**

“**Lipogenesis**” = conversion of excess glucose into ketones, fatty acids, and white fat (triglycerides) stored in adipose & liver. Stimulus = “**insulin**”

“**Lipolysis**” = conversion of white fat (triglycerides) or ketones into molecules that can be used to make ATP, glucose, and glycogen. Stimulus = “**cortisol**”
Lipid Metabolism:

“Lipogenesis” = conversion of excess glucose into white fat (triglycerides) in adipose & liver. Stimulus = “insulin”

1. Extra blood Glucose enters glycolysis to produce pyruvate

2. Pyruvate goes thru conversion into Acetyl CoA

3. Acetyl CoA used by liver to make:
   a) cholesterol – used to make cell membranes, to make steroid hormones, and to make bile.
   
   b) ketones – can be used to make ATP (energy) when no carbohydrates available.
   
   c) fatty acids – get converted into triglycerides (or white fate)
      - Metabolized for energy (ATP) if no carbs in lipolysis.

Lipid Metabolism:

“Lipolysis” = conversion of white fat (triglycerides) into molecules that can be used for energy (ATP).

A) Triglycerides turned into Ketones by liver (process = ketogenesis)
   Ketones metabolized for energy (ATP) if no carbs (process called ketosis)

B) Triglycerides turned into fatty acids, if needed, can be converted back into Acetyl CoA & enter kreb’s cycle to make ATP & H’s

OR Acetyl CoA can be converted back into Pyruvate, and then changed into:
- glucose (gluconeogenesis)
- glucose can be stored as glycogen (glycogenesis)
**Lipid Metabolism, cont...**

**Ketogenesis** = making ketones

**Ketosis** = *use of ketones for energy (lacking carbs)*
Click [HERE](#) for clinical app on ketosis.

**Ketoacidosis** = drop in blood pH from ketosis (BAD!)

**Metabolic acidosis** = metabolizing molecules that drop blood pH.

Click [HERE](#) for blank flow diagram. Click [HERE](#) for key.
Amino acid metabolism

- **Amino acids** = building blocks of protein

- **Essential a.a.** = that which we need to consume in diet because body doesn’t make

- **Nonessential a.a.** = ones our body can make.

- **Excess a.a. converted by liver into pyruvate or other acids. These can be used:**
  - 1) in Kreb’s cycle for ATP (when pyruvate goes thru conversion to make Acetyl CoA)
  - 2) converted to fat (lipogenesis) or glucose (gluconeogenesis)

Un-used a.a. (excess or what body absolutely cannot use)
> liver converts a.a. into Urea and is excreted by kidneys as ammonia.

- blood panels include **BUN** (blood urea nitrogen) to determine kidney function.

- Normal BUN = 10 – 20 mg/dl. Higher BUN called “azotemia” and can indicate excess a.a. metabolism and /or kidney failure.

Click [HERE](#) for blank flow diagram. Click [HERE](#) for key.
Ques:
Metabolism of what molecules can lead to metabolic acidosis?

Answer:
> Amino acids
> Fatty acids
> Ketones (ketoacidosis)
> Lactic acid

Disorder in amino acid metabolism:

**Phenylketonuria (PKU)** – Read online Clinical App:
Genetic condition of mutation in gene for enzyme Phenylalanine hydrolase (PAH).

[Need PAH to metabolize amino acid “phenylalanine”. Without PAH phenylalanine builds up in body and is converted to “phenylketone”, which is excreted in urine.

Phenylketone is toxic, causes seizures.

**Treatment:**
Restrict phenylalanine in diet. (nutrition labels have a warning)
Review

- **Metabolism of lactic acid, lipids, and protein**
- **Lactic acid metabolism** occurs all the time due to skeletal muscle activity
  - Lactic acid in blood causes metabolic acidosis.
  - Liver recycles lactic acid into glucose & glycogen thru the **Cori cycle**. *(Gluconeogensis)*
- **Lipid metabolism** includes making lipids *(lipogenesis)* and breaking them down *(lipolysis)*
  - **Lipogenesis** involves converting excess glucose into pyruvate *(thru glycolysis)*, and then into Acetyl CoA *(thru pyruvate conversion)*
    - Acetyl CoA used by liver to make: cholesterol, ketones, & fatty acids.
    - Fatty acids converted to triglycerides *(white fat)* for storage
  - **Lipolysis** is simply going backwards biochemically from triglycerides to fatty acids & ketones, which can be metabolized for energy OR converted to glucose *(gluconeogenesis)*
- **Amino acids** can be converted by liver to urea for excretion by kidneys as ammonia,
  - Liver can also convert excess a.a. into pyruvate and then to glucose *(gluconeogenesis)*
    - If kidneys not functioning, urea build up in the blood causing **azotemia**.
    - **PKU** = genetic problem metabolizing a.a. phenylalanine. Must avoid phenylalanine in diet because body cannot process it and turns it into toxic phenylketones.